JUVÉDERM® 24HV
Injectable gel

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

JUVÉDERM 24HV injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogenized gel implant. JUVÉDERM 24HV consists of crosslinked hyaluronic acid (HA) produced by *Streptococcus equi* bacteria, formulated to a concentration of 24 mg/mL, and suspended in a physiologic buffer.

2. INTENDED USE/ INDICATIONS

JUVÉDERM 24HV is indicated for injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds).

3. CONTRAINDICATIONS

- JUVÉDERM 24HV is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.

- JUVÉDERM 24HV contains trace amounts of gram positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.

4. WARNINGS

- JUVÉDERM 24HV must not be injected into blood vessels. Introduction of JUVÉDERM 24HV into the vasculature may occlude the vessels and could cause infarction or embolization.

- Use of JUVÉDERM 24HV at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present, should be deferred until the underlying process has been controlled.

- Injection procedure reaction to JUVÉDERM 24HV has been observed as consisting mainly of short-term inflammatory symptoms starting early after treatment and with less than 7 days duration. Refer to the ADVERSE EVENTS section for details.

5. PRECAUTIONS

- JUVÉDERM 24HV is packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged.

- Based on preclinical studies, patients should be limited to 20 mL of JUVÉDERM 24HV per 60 kg (130 lbs) body mass per year. The safety of injecting greater amounts has not been established.

- The safety and effectiveness of JUVÉDERM 24HV for the treatment of anatomic regions other than facial wrinkles and folds (e.g., lips) have not been established in controlled clinical studies.

- As with all transcutaneous procedures, JUVÉDERM 24HV implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.

- The safety of JUVÉDERM 24HV for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.

- The safety of JUVÉDERM 24HV in patients with known susceptibility to keloid formation, hypertrophic scarring and pigmentation disorders has not been studied.

- JUVÉDERM 24HV should be used with caution in patients on immunosuppressive therapy.

- Patients who are using substances that can prolong bleeding, such as aspirin, non-steroidal anti-inflammatory drugs and warfarin may, as with any injection, experience increased bruising or bleeding at injection sites.

- After use, treatment syringes and needles may be potential biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state and federal requirements.

- JUVÉDERM 24HV is a clear, colorless gel without particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe; notify INAMED Corporation at (800) 624-4261.

- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with JUVÉDERM 24HV, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if JUVÉDERM 24HV is administered before the skin has healed completely after such a procedure.

6. ADVERSE EVENTS

A. Clinical Evaluation of JUVÉDERM 24HV

In a randomized, controlled clinical trial to evaluate safety and effectiveness, 146 subjects were injected with JUVÉDERM 24HV in one nasolabial fold (NLF) and ZYPLAST® in the contralateral NLF. Pre-printed diary forms were used by subjects to record specific signs and symptoms experienced during each of the first 14 days (Day 0 through Day 13) after initial and touch-up treatments. Subjects were instructed to rate each common treatment response listed on the diary as "Mild," "Moderate," "Severe," or "None." Injection site responses reported by >5% of subjects in either treatment group are summarized in Tables 1 and 2.

Table 1 – Injection Site Responses by Maximum Severity Occurring in >5% of Treated Subjects (Number / % of Subject NLFs)

Injection Site Responses	TOTALS		JUVÉDERM 24HV (N*=146 NLFS)			Zyplast (N*=146 NLFs)		
	JUVÉDERM 24HV n‡ %	Zyplast n‡ %	Mild n‡ %	Mod† n‡ %	Severe n‡ %	Mild n‡ %	Mod† n‡ %	Severe n‡ %
Redness	136 93%	130 89%	72 49%	48 33%	16 11%	69 47%	45 31%	16 11%
Pain/Tenderness	131 90%	128 88%	74 51%	45 31%	12 8%	87 60%	34 23%	7 5%
Firmness	129 88%	127 87%	66 45%	53 36%	10 7%	60 41%	56 38%	11 8%
Swelling	125 86%	122 84%	60 41%	54 37%	11 8%	77 53%	37 25%	8 5%
Lumps/Bumps	115 79%	122 84%	61 42%	45 31%	9 6%	66 45%	42 29%	14 10%
Bruising	86 59%	80 55%	43 29%	29 20%	14 10%	47 32%	27 18%	6 4%
Itching	52 36%	53 36%	42 29%	5 3%	5 3%	43 29%	7 5%	3 2%
Discoloration	48 33%	49 34%	31 21%	11 8%	6 4%	31 21%	15 10%	3 2%

* Number of subject NLFs treated with the respective device
† Mod = Moderate
‡ Number of subject NLFs with each specific injection site response

Table 2 – Duration of Injection Site Responses Occurring in > 5% of Treated Subjects (Number / % of Subject NLFs)

Injection Site Response	JUVÉDERM 24HV (N*=146 NLFs) n† %				Zyplast (N*=146 NLFs) n† %			
Duration‡	≤3 Days	4-7 Days	8-14 Days	>14 Days	≤3 Days	4-7 Days	8-14 Days	>14 Days
Redness	60 41%	50 34%	8 5%	18 12%	46 32%	46 32%	10 7%	28 19%
Pain/Tenderness	61 42%	46 32%	18 12%	6 4%	49 34%	53 36%	14 10%	12 8%
Firmness	29 20%	34 23%	20 14%	46 32%	25 17%	28 19%	20 14%	54 37%
Swelling	38 26%	48 33%	22 15%	17 12%	54 37%	38 26%	20 14%	10 7%
Lumps/Bumps	26 18%	32 22%	18 12%	39 27%	16 11%	18 12%	19 13%	69 47%
Bruising	29 20%	28 19%	24 16%	5 3%	35 24%	27 18%	10 7%	8 5%
Itching	25 17%	15 10%	7 5%	5 3%	21 14%	17 12%	4 3%	11 8%
Discoloration	22 15%	12 8%	4 3%	10 7%	26 18%	9 6%	3 2%	11 8%

*Number of subject NLFs treated with the respective device
†Number of subject NLFs with each specific injection site response by maximum duration
‡Duration refers to number of days from symptom onset until resolution, irrespective of date of implantation.

Local injection site responses were recorded in subjects' diaries one or more times for 99% of JUVÉDERM-treated NLFs and 98% of Zyplast-treated NLFs. Subjects' scores for both products were predominantly Mild or Moderate in intensity, and their duration was short lasting (7 days or less). JUVÉDERM 24HV injection site responses reported by greater than 1% of subjects and not noted in the above tables were skin dryness and peeling. No clinically meaningful differences in the safety profiles of JUVÉDERM 24HV and Zyplast were found during the study.

B. Other Safety Data

In two additional randomized U.S. clinical studies of other JUVÉDERM formulations with a total of 293 subjects, the safety profile was similar to that described above for JUVÉDERM 24HV.

Post market safety surveillance of JUVÉDERM in countries outside the U.S. indicates that the most common adverse events include swelling, redness, discoloration, and bruising.

7. CLINICAL STUDY

A. Study Design

A prospective double-blind, randomized, within-subject controlled, multi-center clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM 24HV in the treatment of moderate to severe wrinkles. Subjects underwent treatment with JUVÉDERM 24HV in one NLF and the control implant (Zyplast bovine collagen) in the opposite NLF.

Up to 3 bilateral treatments (initial treatment and up to 2 touch-up treatments), approximately 2 weeks apart, were allowed. At 2 and 4 weeks after each treatment, the Independent Expert Reviewer (IER) assessed the level of correction achieved. If correction was less than optimal after the first or second treatment, the Investigator re-treated the under-corrected NLFs using the same respective treatment materials as in the initial treatment. The IER and the subject remained masked to the randomized treatment assignment.

Routine follow-up visits for safety and effectiveness occurred at Days 3 and 7 and Week 2 after each treatment, and at 4, 8, 12, 16, 20, and 24 weeks after the last treatment. Standardized facial photography was performed for documentation purposes. The Investigator and the IER independently evaluated the severity of the subject's NLFs using a validated 5-point (range 0 to 4) photographic NLF severity scale. The subject made independent self-assessments of NLF severity using a non-photographic 5-point grading scale.

B. Study Endpoints

The primary effectiveness end point for the study was the IER's NLF severity score over the post-treatment follow-up period. Effectiveness of device treatment was demonstrated by a lowering of the NLF severity score. Additional analyses included the subject's and the Investigator's live NLF severity assessments.

C. Subject Demographics

A total of 146 subjects (31 to 75 years of age) were randomized and treated, and 140 (96%) completed the 6-month follow-up period. Prior to enrollment, 87 (60%) had previous experience with other facial dermal treatments (e.g. alpha hydroxy agents, BOTOX® Cosmetic, microdermabrasion or retinoic acid).

Subject demographics and pre-treatment characteristics of the JUVÉDERM 24HV effectiveness population are presented in Table 3.

Table 3 – Demographics and Pretreatment Characteristics of the Effectiveness Population (Number / % of Subjects)

N = 146

Gender (Number / %)		
Female	135	92%
Male	11	8%
Ethnicity (Number / %)		
Caucasian	105	72%
African American	18	12%
Hispanic	15	10%
Asian	7	5%
Other	1	1%
Fitzpatrick Skin Phototype (Number / %)		
I	4	3%
II	34	23%
III	55	38%
IV	24	16%
V	24	16%
VI	5	3%
Mean Baseline NLF Severity Score*		
JUVÉDERM 24HV NLF	2.6	
Zyplast NLF	2.6	

*NLF Severity was ranked on a 5-point scale from None (0) to Extreme (4)

D. Effectiveness Results

The primary effectiveness results for JUVÉDERM 24HV based on the IER's assessment of NLF severity are presented in Table 4.

Table 4 – Effectiveness Summary
Independent Expert Reviewer's
NLF Severity Scores

		JUVÉDERM 24HV (N*=146 NLFs)		Control** (N*=146 NLFs)	
	n[§]	NLF Severity[†]	Improvement since Baseline[†]	NLF Severity[†]	Improvement since Baseline[†]
Baseline	146	2.6	–	2.6	–
Week 2	142	0.6	2.0	0.7	1.9
Week 12	129	0.9	1.7	1.6	1.0
Week 24	138	1.3	1.3	2.3	0.3

* Number of subject NLFs treated with the respective device
** A commercially available injectable bovine collagen implant
§ Number of subjects NLFs with data at baseline and the specified time point
† Mean score

Throughout the 24-week study period, JUVÉDERM 24HV provided a clinically and statistically significant improvement in NLF severity. Clinical superiority was achieved at Week 24 for JUVÉDERM 24HV over Zyplast with mean NLF severity of 1.3 and 2.3, respectively (P <0.0001). Additionally, subject assessments for product preference favored JUVÉDERM 24HV: 88% preferred the JUVÉDERM-treated NLF over the Zyplast-treated NLF.

8. INSTRUCTIONS FOR USE

A. <u>To Attach Needle to Syringe</u>

- To assure proper needle attachment, use needles provided.
- Peel sealed cover off needle guard.
- Remove luer-lock end closure (tip cap) from syringe.
- Attach needle to syringe and twist to secure. Fully seat hub of needle in syringe. Do not over-tighten, as this may break the needle and/or dislodge the syringe.
- Pull off the needle guard to expose needle.

B. Physician Instructions

1. JUVEDERM 24HV is a highly crosslinked formulation that can be injected using a 30 G needle for more versatility in contouring and volumizing of facial wrinkles and folds . Prior to treatment with JUVÉDERM 24HV, the patient's medical history should be obtained and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration. Patients also should be advised that supplemental "touch-up" implantations may be required to achieve and maintain maximum correction.

2. The patient's soft tissue deficiencies should be characterized with regard to etiology, distensibility, stress at the site, and depth of lesion. Depending on the type of skin, best results are obtained when the defect is readily distensible and correction can be visualized by manual manipulation (stretching) of the skin. Pretreatment photographs are recommended.

3. Topical or injectable anesthesia may be used to manage pain during and after injection.

4. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be swabbed with alcohol or other antiseptic. Prior to injecting JUVÉDERM 24HV, depress the plunger rod until the product flows out of the needle.

5. The injection technique of JUVÉDERM 24HV with regard to the angle and orientation of the bevel, the depth of injection, and the quantity administered may vary. A linear threading technique, serial puncture injections, or a combination of the two have been used to achieve optimal results. If JUVÉDERM 24HV is injected too superficially, this may result in visible lumps and/or discoloration.

6. Inject JUVÉDERM 24HV applying even pressure on the plunger rod while slowly pulling the needle backwards. The wrinkle should be lifted and eliminated by the end of the injection. It is important that the injection is stopped just before the needle is pulled out of the skin to prevent material from leaking out or ending up too superficially in the skin.

7. The typical total volume of JUVÉDERM 24HV to achieve optimal correction is 1.6 mL per treatment site.

8. Correct to 100% of the desired volume effect. Do not overcorrect. The degree and duration of the correction depend on the character of the defect treated, the tissue stress at the implant site, the depth of the implant in the tissue and the injection technique. Markedly indurated defects may be difficult to correct.

9. If immediate blanching occurs, the injection should be stopped and the area massaged until it returns to a normal color.

10. When injection is completed, the treated site should be gently massaged so that it conforms to the contour of the surrounding tissues. If overcorrection occurs, massage the area

between your fingers or against an underlying superficial bone to obtain optimal results.

11. With patients who have localized swelling, the degree of correction is sometimes difficult to judge at the time of treatment. In these cases, it is better to invite the patient to a touch-up session after 1-2 weeks.

12. Patients may have mild to moderate injection site responses, which typically resolve in a few days. If the treated area is swollen immediately after the injection, an ice pack can be applied to the site for a short period.

13. After the initial treatment, an additional treatment of JUVÉDERM 24HV (from 1 to 2 weeks later) may be necessary to achieve the desired level of correction. If the wrinkle needs further treatment, the same procedure should be repeated until a satisfactory result is obtained. The need for an additional treatment may vary from patient to patient and is dependent upon a variety of factors such as wrinkle severity, skin elasticity and dermal thickness at the treatment site.

14. The physician should instruct the patient to promptly report to her/him any evidence of problems possibly associated with the use of JUVÉDERM 24HV.

C. Patient Instructions

It is recommended that the following information be shared with patients:

- Within the first 24 hours, patients should avoid strenuous exercise, extensive sun or heat exposure and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites.
- To report an adverse reaction, phone the Product Support Department, INAMED Corporation, (800) 624-4261.

9. HOW SUPPLIED

JUVÉDERM 24HV is supplied in individual treatment syringes with 30-gauge needles for single patient use and ready for injection (implantation). The volume in each syringe is as stated on the syringe label and on the carton. The contents of the syringe are sterile and non-pyrogenic. Do not resterilize. Do not use if package is opened or damaged.

10. STORAGE

JUVÉDERM 24HV should be stored at room temperature (up to 25°C / 77°F). DO NOT FREEZE.

JUVÉDERM 24HV has a clear appearance. In the event that a syringe contains material that is not clear, do not use the syringe; notify INAMED Corporation immediately at (800) 624-4261.

To place an order, contact INAMED Corporation at (800) 624-4261.

Manufactured by:

Corneal
31, rue des Colonnes du Trône
75012 Paris France

Distributed by:

INAMED Aesthetics
5540 Ekwill Street
Santa Barbara, CA 93111 USA
(800) 624-4261

Juvéderm® 24HV

Patient Information Labeling

What is it? Juvéderm 24HV is a colorless hyaluronic acid gel that is injected into facial tissue to smooth wrinkles and folds, especially around the nose and mouth. Hyaluronic acid is a naturally occurring sugar found in the human body. The role of hyaluronic acid in the skin is to deliver nutrients, hydrate the skin by holding in water, and to act as a cushioning agent.

What does it do? Juvéderm 24HV temporarily adds volume to facial tissue and restores a smoother appearance to the face.

How is it used? Juvéderm 24HV is injected into areas of facial tissue where moderate to severe facial wrinkles and folds occur. Juvéderm 24HV temporarily adds volume to the skin and may give the appearance of a smoother surface.

What will it accomplish? Juvéderm 24HV will help to smooth moderate to severe facial wrinkles and folds. Most patients need one treatment to achieve optimal wrinkle smoothing, and the results last about six months.

What are possible side effects?
Most side effects are mild or moderate in nature, and their duration is short lasting (7 days or less). The most common side effects include but are not limited to temporary injection site reactions such as: redness, pain/tenderness, firmness, swelling, lumps/bumps, bruising, itching, and discoloration.

As with all skin injection procedures there is a risk of infection.

Are there any reasons why I should not receive Juvéderm 24HV?
Your physician will ask about your medical history to determine if you are an appropriate candidate for treatment. Juvéderm 24HV should not be used in patients who have:

- Severe allergies marked by a history of anaphylaxis or history or presence of multiple severe allergies
- Patients with a history of allergies to gram-positive bacterial proteins

What should my physician advise me about?
The following are important treatment considerations for you to discuss with your physician and understand in order to help avoid unsatisfactory results and complications.

- Patients who are using substances that can prolong bleeding, such as aspirin or ibuprofen, as with any injection, may experience increased bruising or bleeding at injection site. You should inform your physician before treatment if you are using these types of substances.
- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with Juvéderm 24HV, there is a possible risk of an inflammatory reaction at the treatment site.
- Juvéderm 24HV should be used with caution in patients on immunosuppressive therapy, or therapy used to decrease the body's immune response, as there may be an increased risk of infection.
- The safety of Juvéderm 24HV for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.
- The safety of Juvéderm 24HV in patients with a history of excessive scarring (e.g. hypertrophic scarring and keloid formations) and pigmentation disorders has not been studied.

What should my physician warn me about?
The safety and effectiveness of Juvéderm 24HV for the treatment of areas other than facial wrinkles and folds (such as lips) have not been established in controlled clinical studies.

What did the clinical study show?
In a U.S. clinical study 146 subjects were followed for 24 weeks after injection with Juvéderm 24HV in one nasolabial fold and Zyplast® (bovine-based collagen) in the other. The percentage of subjects who reported common injection site responses are presented in the table below.

Injection Site Responses*
N = 146

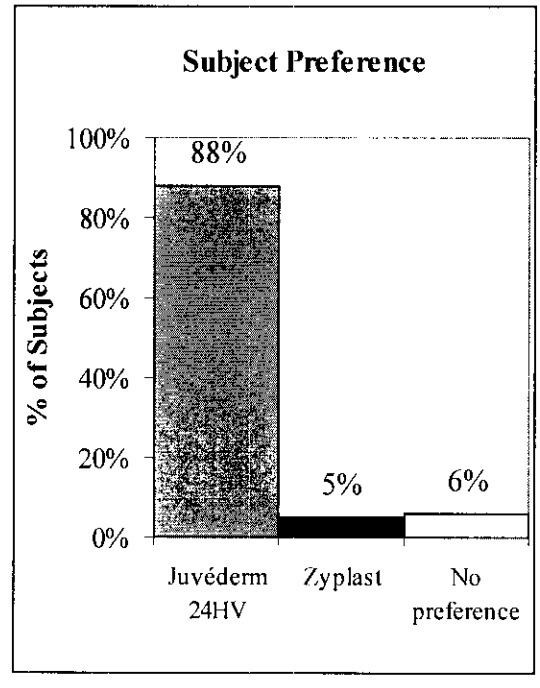
Injection Site Responses	Juvéderm 24HV		Zyplast	
	n**	%	n**	%
Redness	136	93%	130	89%
Pain/Tenderness	131	90%	128	88%
Firmness	129	88%	127	87%
Swelling	125	86%	122	84%
Lumps/Bumps	115	79%	122	84%
Bruising	86	59%	80	55%
Itching	52	36%	53	36%
Discoloration	48	33%	49	34%

*occurring in > 5% of subjects

** Number of subject NLFs with each specific injection site response

Injection site responses were similar in duration and frequency for the Juvéderm 24HV and Zyplast treated sides, were usually mild or moderate in severity, did not require intervention, and lasted 7 days or less.

Juvéderm 24HV was found to provide a more persistent wrinkle correction than Zyplast over the 24-week course of the study. The percentage of subjects who maintained improvement with Juvéderm 24HV at 24 weeks was 88% compared to 36% with Zyplast. At the conclusion of the study, 129 (88%) of the 146 subjects expressed a preference for Juvéderm 24HV, while only 8 (5%) expressed a preference for Zyplast, and 9 (6%) had no preference.



Do the injections hurt?
Injections may cause some discomfort during and after the injection. Juvéderm 24HV is injected directly into the skin using a fine needle to reduce injection discomfort. Physicians may choose to numb (anesthetize) the treatment area to further minimize discomfort.

What should I expect following the procedure?
Your physician will tell you what to expect following treatment with Juvéderm 24HV. Within the first 24 hours, you should avoid strenuous exercise, extensive sun or heat exposure and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites. If there is swelling, you may need to place an ice pack over the swollen area. You should ask your physician when makeup may be applied after your treatment.

Does the correction last forever?
No. Correction is temporary; therefore, touch-up injections as well as repeat injections are usually needed to maintain optimal correction.

What other treatments are available to me?
Other treatments for dermal soft tissue augmentation include bovine-based collagen and other hyaluronic acid-based dermal fillers. Aside from these treatments, additional options for the correction of lines and wrinkles do exist, including facial creams, Botox® Cosmetic, chemical peels, and laser skin surface treatments, and may be discussed with your physician.

When should I notify my physician?
Be sure to report any redness and/or visible swelling that lasts for more than a few days or any other symptoms that cause you concern to your physician and/or contact INAMED Product Support at (800) 624-4261.

For further questions and information please call 1-800-766-0171.

M#### .Rev ## MM/YY

JUVÉDERM® 30
Injectable gel

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

JUVÉDERM 30 injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogenized gel implant. JUVÉDERM 30 consists of crosslinked hyaluronic acid (HA) produced by *Streptococcus equi* bacteria, formulated to a concentration of 24 mg/mL, and suspended in a physiologic buffer.

2. INTENDED USE/ INDICATIONS

JUVÉDERM 30 is indicated for injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds).

3. CONTRAINDICATIONS

- JUVÉDERM 30 is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.

- JUVÉDERM 30 contains trace amounts of gram positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.

4. WARNINGS

- JUVÉDERM 30 must not be injected into blood vessels. Introduction of JUVÉDERM 30 into the vasculature may occlude the vessels and could cause infarction or embolization.

- Use of JUVÉDERM 30 at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present, should be deferred until the underlying process has been controlled.

- Injection procedure reaction to JUVÉDERM 30 has been observed as consisting mainly of short-term inflammatory symptoms starting early after treatment and with less than 7 days duration. Refer to the ADVERSE EVENTS section for details.

5. PRECAUTIONS

- JUVÉDERM 30 is packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged.

- Based on preclinical studies, patients should be limited to 20 mL of JUVÉDERM 30 per 60 kg (130 lbs) body mass per year. The safety of injecting greater amounts has not been established.

- The safety and effectiveness of JUVÉDERM 30 for the treatment of anatomic regions other than facial wrinkles and folds (e.g., lips) have not been established in controlled clinical studies.

- As with all transcutaneous procedures, JUVÉDERM 30 implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.

- The safety of JUVÉDERM 30 for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.

- The safety of JUVÉDERM 30 in patients with known susceptibility to keloid formation, hypertrophic scarring and pigmentation disorders has not been studied.

- JUVÉDERM 30 should be used with caution in patients on immunosuppressive therapy.

- Patients who are using substances that can prolong bleeding, such as aspirin, non-steroidal anti-inflammatory drugs and warfarin may, as with any injection, experience increased bruising or bleeding at injection sites.

- After use, treatment syringes and needles may be potential biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state and federal requirements.

- JUVÉDERM 30 is a clear, colorless gel without particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe; notify INAMED Corporation at (800) 624-4261.

- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with JUVÉDERM 30, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if JUVÉDERM 30 is administered before the skin has healed completely after such a procedure.

6. ADVERSE EVENTS

A. Clinical Evaluation of JUVÉDERM 30

In a randomized, controlled clinical trial to evaluate safety and effectiveness, 149 subjects were injected with JUVÉDERM 30 in one nasolabial fold (NLF) and ZYPLAST® in the contralateral NLF. Pre-printed diary forms were used by subjects to record specific signs and symptoms experienced during each of the first 14 days (Day 0 through Day 13) after initial and touch-up treatments. Subjects were instructed to rate each common treatment response listed on the diary as "Mild," "Moderate," "Severe," or "None." Injection site responses reported by >5% of subjects in either treatment group are summarized in Tables 1 and 2.

Table 1 – Injection Site Responses by Maximum Severity Occurring in >5% of Treated Subjects (Number / % of Subject NLFs)

Injection Site Responses	TOTALS		JUVÉDERM 30 (N*=149 NLFS)			Zyplast (N*=149 NLFs)		
	JUVÉDERM 30 n‡ %	Zyplast n‡ %	Mild n‡ %	Mod† n‡ %	Severe n‡ %	Mild n‡ %	Mod† n‡ %	Severe n‡ %
Firmness	136 91%	132 89%	62 42%	66 44%	8 5%	60 40%	63 42%	9 6%
Redness	134 90%	132 89%	73 49%	44 30%	17 11%	63 42%	54 36%	15 10%
Swelling	132 89%	128 86%	65 44%	58 39%	9 6%	81 54%	43 29%	4 3%
Pain/Tenderness	129 87%	128 86%	74 50%	45 30%	10 7%	91 61%	33 22%	4 3%
Lumps/Bumps	123 83%	122 82%	65 44%	49 33%	9 6%	64 43%	50 34%	8 5%
Bruising	91 61%	79 53%	49 33%	27 18%	15 10%	51 34%	25 17%	3 2%
Discoloration	46 31%	43 29%	36 24%	7 5%	3 2%	37 25%	5 3%	1 1%
Itching	42 28%	52 35%	31 21%	10 7%	1 1%	38 26%	11 7%	3 2%

* Number of subject NLFs treated with the respective device
† Mod = Moderate
‡ Number of subject NLFs with each specific injection site response

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Table 2 – Duration of Injection Site Responses Occurring in > 5% of Treated Subjects (Number / % of Subject NLFs)

Injection Site Response	JUVÉDERM 30 (N*=149 NLFs) n† %				Zyplast (N*=149 NLFs) n† %			
Duration‡	≤3 Days	4-7 Days	8-14 Days	>14 Days	≤3 Days	4-7 Days	8-14 Days	>14 Days
Firmness	40 27%	26 17%	21 14%	49 33%	34 23%	28 19%	14 9%	56 38%
Redness	68 46%	40 27%	14 9%	12 8%	51 34%	37 25%	14 9%	30 20%
Swelling	48 32%	44 30%	28 19%	12 8%	63 42%	43 29%	14 9%	8 5%
Pain/Tenderness	73 49%	36 24%	15 10%	5 3%	60 40%	39 26%	21 14%	8 5%
Lumps/Bumps	38 26%	27 18%	21 14%	37 25%	16 11%	21 14%	21 14%	64 43%
Bruising	30 20%	34 23%	24 16%	3 2%	41 28%	30 20%	7 5%	1 1%
Discoloration	31 21%	8 5%	4 3%	3 2%	26 17%	11 7%	3 2%	3 2%
Itching	23 15%	14 9%	3 2%	2 1%	24 16%	12 8%	9 6%	7 5%

*Number of subject NLFs treated with the respective device
†Number of subject NLFs with each specific injection site response by maximum duration
‡Duration refers to number of days from symptom onset until resolution, irrespective of date of implantation.

Local injection site responses were recorded in subjects' diaries one or more times for 98% of JUVÉDERM-treated NLFs and 99% of Zyplast-treated NLFs. Subjects' scores for both products were predominantly Mild or Moderate in intensity, and their duration was short lasting (7 days or less). JUVÉDERM 30 injection site responses reported by greater than 1% of subjects and not noted in the above tables were skin peeling and skin wrinkling. No clinically meaningful differences in the safety profiles of JUVÉDERM 30 and Zyplast were found during the study.

B. Other Safety Data

In two additional randomized U.S. clinical studies of other JUVÉDERM formulations with a total of 290 subjects, the safety profile was similar to that described above for JUVÉDERM 30.

Post market safety surveillance of JUVÉDERM in countries outside the U.S. indicates that the most common adverse events include swelling, redness, discoloration, and bruising.

7. CLINICAL STUDY

A. Study Design

A prospective double-blind, randomized, within-subject controlled, multi-center clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM 30 in the treatment of moderate to severe wrinkles. Subjects underwent treatment with JUVÉDERM 30 in one NLF and the control implant (Zyplast bovine collagen) in the opposite NLF.

Up to 3 bilateral treatments (initial treatment and up to 2 touch-up treatments), approximately 2 weeks apart, were allowed. At 2 and 4 weeks after each treatment, the Independent Expert Reviewer (IER) assessed the level of correction achieved. If correction was less than optimal after the first or second treatment, the Investigator re-treated the under-corrected NLFs using the same respective treatment materials as in the initial treatment. The IER and the subject remained masked to the randomized treatment assignment.

Routine follow-up visits for safety and effectiveness occurred at Days 3 and 7 and Week 2 after each treatment, and at 4, 8, 12, 16, 20, and 24 weeks after the last treatment. Standardized facial photography was performed for documentation purposes. The Investigator and the IER independently evaluated the severity of the subject's NLFs using a validated 5-point (range 0 to 4) photographic NLF severity scale. The subject made independent self-assessments of NLF severity using a non-photographic 5-point grading scale.

B. Study Endpoints

The primary effectiveness end point for the study was the IER's NLF severity score over the post-treatment follow-up period. Effectiveness of device treatment was demonstrated by a lowering of the NLF severity score. Additional analyses included the subject's and the Investigator's live NLF severity assessments.

C. Subject Demographics

A total of 147 subjects (30 to 70 years of age) were randomized and treated, and 143 (97%) completed the 6-month follow-up period. Prior to enrollment, 90 (61%) had previous experience with other facial dermal treatments (e.g. alpha hydroxy agents, BOTOX® Cosmetic, microdermabrasion or retinoic acid).

Subject demographics and pre-treatment characteristics of the JUVÉDERM 30 effectiveness population are presented in Table 3.

Table 3 – Demographics and Pretreatment Characteristics of the Effectiveness Population (Number / % of Subjects)

N = 147

Gender (Number / %)		
Female	136	93%
Male	11	7%
Ethnicity (Number / %)		
Caucasian	115	78%
African American	14	10%
Hispanic	16	11%
Asian	1	1%
Other	1	1%
Fitzpatrick Skin Phototype (Number / %)		
I	6	4%
II	39	27%
III	48	33%
IV	34	23%
V	15	10%
VI	5	3%
Mean Baseline NLF Severity Score*		
JUVÉDERM 30 NLF	2.5	
Zyplast NLF	2.6	

*NLF Severity was ranked on a 5-point scale from None (0) to Extreme (4)

D. Effectiveness Results

The primary effectiveness results for JUVÉDERM 30 based on the IER's assessment of NLF severity are presented in Table 4.

Table 4 – Effectiveness Summary
Independent Expert Reviewer's
NLF Severity Scores

		Juvéderm 30 (N*=147 NLFs)		Control ** (N*=147 NLFs)	
	n§	NLF Severity†	Improvement since Baseline†	NLF Severity†	Improvement since Baseline†
Baseline	147	2.5	–	2.6	–
Week 2	146	0.6	1.9	0.7	1.8
Week 12	133	0.9	1.6	1.5	1.0
Week 24	143	1.4	1.2	2.1	0.5

* Number of subject NLFs treated with the respective device
** A commercially available injectable bovine collagen implant
§ Number of subjects NLFs with data at baseline and the specified time point
† Mean score

Throughout the 24-week study period, JUVÉDERM 30 provided a clinically and statistically significant improvement in NLF severity. Non-inferiority was achieved at Week 24 for JUVÉDERM 30 over Zyplast with mean NLF severity of 1.4 and 2.1, respectively (P <0.0001). Additionally, subject assessments for product preference favored JUVÉDERM 30: 78% preferred the JUVÉDERM-treated NLF over the Zyplast-treated NLF.

8. INSTRUCTIONS FOR USE

A. To Attach Needle to Syringe

- To assure proper needle attachment, use needles provided.
- Peel sealed cover off needle guard.
- Remove luer-lock end closure (tip cap) from syringe.
- Attach needle to syringe and twist to secure. Fully seat hub of needle in syringe. Do not over-tighten, as this may break the needle and/or dislodge the syringe.
- Pull off the needle guard to expose needle.

B. Physician Instructions

1. JUVÉDERM 30 is a highly crosslinked formulation, injected using a 27G needle, for subtle correction of facial wrinkles and folds. Prior to treatment with JUVÉDERM 30, the patient's medical history should be obtained and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration. Patients also should be advised that supplemental "touch-up" implantations may be required to achieve and maintain maximum correction.

2. The patient's soft tissue deficiencies should be characterized with regard to etiology, distensibility, stress at the site, and depth of lesion. Depending on the type of skin, best results are obtained when the defect is readily distensible and correction can be visualized by manual manipulation (stretching) of the skin. Pretreatment photographs are recommended.

3. Topical or injectable anesthesia may be used to manage pain during and after injection.

4. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be swabbed with alcohol or other antiseptic. Prior to injecting JUVÉDERM 30, depress the plunger rod until the product flows out of the needle.

5. The injection technique of JUVÉDERM 30 with regard to the angle and orientation of the bevel, the depth of injection, and the quantity administered may vary. A linear threading technique, serial puncture injections, or a combination of the two have been used to achieve optimal results. If JUVÉDERM 30 is injected too superficially, this may result in visible lumps and/or discoloration.

6. Inject JUVÉDERM 30 applying even pressure on the plunger rod while slowly pulling the needle backwards. The wrinkle should be lifted and eliminated by the end of the injection. It is important that the injection is stopped just before the needle is pulled out of the skin to prevent material from leaking out or ending up too superficially in the skin.

7. The typical total volume of JUVÉDERM 30 to achieve optimal correction is 1.6 mL per treatment site.

8. Correct to 100% of the desired volume effect. Do not overcorrect. The degree and duration of the correction depend on the character of the defect treated, the tissue stress at the implant site, the depth of the implant in the tissue and the injection technique. Markedly indurated defects may be difficult to correct.

9. If immediate blanching occurs, the injection should be stopped and the area massaged until it returns to a normal color.

10. When injection is completed, the treated site should be gently massaged so that it conforms to the contour of the surrounding tissues. If overcorrection occurs, massage the area between your fingers or against an underlying superficial bone to obtain optimal results.

11. With patients who have localized swelling, the degree of correction is sometimes difficult to judge at the time of treatment. In these cases, it is better to invite the patient to a touch-up session after 1-2 weeks.

12. Patients may have mild to moderate injection site responses, which typically resolve in a few days. If the treated area is swollen immediately after the injection, an ice pack can be applied to the site for a short period.

13. After the initial treatment, an additional treatment of JUVÉDERM 30 (from 1 to 2 weeks later) may be necessary to achieve the desired level of correction. If the wrinkle needs further treatment, the same procedure should be repeated until a satisfactory result is obtained. The need for an additional treatment may vary from patient to patient and is dependent upon a variety of factors such as wrinkle severity, skin elasticity and dermal thickness at the treatment site.

14. The physician should instruct the patient to promptly report to her/him any evidence of problems possibly associated with the use of JUVÉDERM 30.

C. Patient Instructions

It is recommended that the following information be shared with patients:

- Within the first 24 hours, patients should avoid strenuous exercise, extensive sun or heat exposure and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites.
- To report an adverse reaction, phone the Product Support Department, INAMED Corporation, (800) 624-4261.

9. HOW SUPPLIED

JUVÉDERM 30 is supplied in individual treatment syringes with 27-gauge needles for single patient use and ready for injection (implantation). The volume in each syringe is as stated on the syringe label and on the carton. The contents of the syringe are sterile and non-pyrogenic. Do not resterilize. Do not use if package is opened or damaged.

10. STORAGE

JUVÉDERM 30 should be stored at room temperature (up to 25°C / 77°F). DO NOT FREEZE.

JUVÉDERM 30 has a clear appearance. In the event that a syringe contains material that is not clear, do not use the syringe; notify INAMED Corporation immediately at (800) 624-4261.

To place an order, contact INAMED Corporation at (800) 624-4261.

Manufactured by:

Corneal
31, rue des Colonnes du Trône
75012 Paris France

Distributed by:

INAMED Aesthetics
5540 Ekwill Street
Santa Barbara, CA 93111 USA
(800) 624-4261

Juvéderm® 30

Patient Information Labeling

What is it? Juvéderm 30 is a colorless hyaluronic acid gel that is injected into facial tissue to smooth wrinkles and folds, especially around the nose and mouth. Hyaluronic acid is a naturally occurring sugar found in the human body. The role of hyaluronic acid in the skin is to deliver nutrients, hydrate the skin by holding in water, and to act as a cushioning agent.

What does it do? Juvéderm 30 temporarily adds volume to facial tissue and restores a smoother appearance to the face.

How is it used? Juvéderm 30 is injected into areas of facial tissue where moderate to severe facial wrinkles and folds occur. Juvéderm 30 temporarily adds volume to the skin and may give the appearance of a smoother surface.

What will it accomplish? Juvéderm 30 will help to smooth moderate to severe facial wrinkles and folds. Most patients need one treatment to achieve optimal wrinkle smoothing, and the results last about six months.

What are possible side effects?
Most side effects are mild or moderate in nature, and their duration is short lasting (7 days or less). The most common side effects include but are not limited to temporary injection site reactions such as: redness, pain/tenderness, firmness, swelling, lumps/bumps, bruising, itching, and discoloration.

As with all skin injection procedures there is a risk of infection.

Are there any reasons why I should not receive Juvéderm 30?
Your physician will ask about your medical history to determine if you are an appropriate candidate for treatment. Juvéderm 30 should not be used in patients who have:

- Severe allergies marked by a history of anaphylaxis or history or presence of multiple severe allergies
- Patients with a history of allergies to gram-positive bacterial proteins

What should my physician advise me about?
The following are important treatment considerations for you to discuss with your physician and understand in order to help avoid unsatisfactory results and complications.

- Patients who are using substances that can prolong bleeding, such as aspirin or ibuprofen, as with any injection, may experience increased bruising or bleeding at injection site. You should inform your physician before treatment if you are using these types of substances.
- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with Juvéderm 30, there is a possible risk of an inflammatory reaction at the treatment site.
- Juvéderm 30 should be used with caution in patients on immunosuppressive therapy, or therapy used to decrease the body's immune response, as there may be an increased risk of infection.
- The safety of Juvéderm 30 for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.
- The safety of Juvéderm 30 in patients with a history of excessive scarring (e.g. hypertrophic scarring and keloid formations) and pigmentation disorders has not been studied.

What should my physician warn me about?
The safety and effectiveness of Juvéderm 30 for the treatment of areas other than facial wrinkles and folds (such as lips) have not been established in controlled clinical studies.

What did the clinical study show?
In a U.S. clinical study 149 subjects were followed for 24 weeks after injection with Juvéderm 30 in one nasolabial fold and Zyplast® (bovine-based collagen) in the other. The percentage of subjects who reported common injection site responses are presented in the table below.

Injection Site Responses*
N = 149

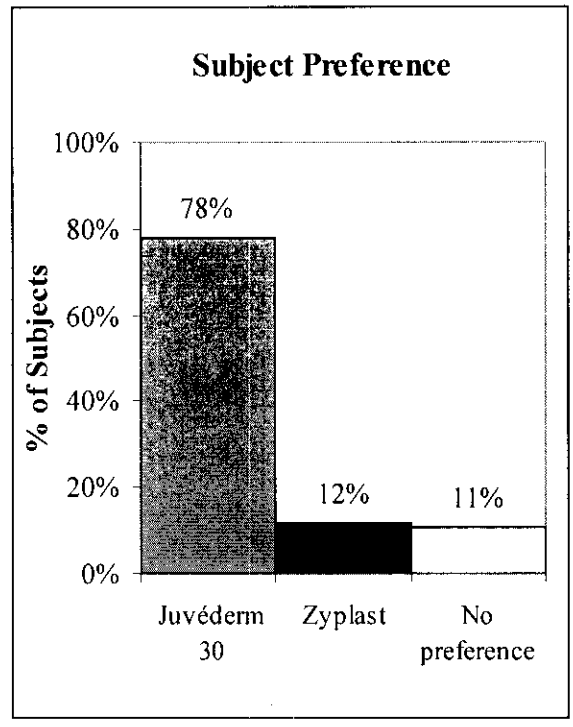
Injection Site Responses	Juvéderm 30		Zyplast	
	n**	%	n**	%
Firmness	136	91%	132	89%
Redness	134	90%	132	89%
Swelling	132	89%	128	86%
Pain/Tenderness	129	87%	128	86%
Lumps/Bumps	123	83%	122	82%
Bruising	91	61%	79	53%
Discoloration	46	31%	43	29%
Itching	42	28%	52	35%

*occurring in > 5% of subjects

** Number of subject NLFs with each specific injection site response

Injection site responses were similar in duration and frequency for the Juvéderm 30 and Zyplast treated sides, were usually mild or moderate in severity, did not require intervention, and lasted 7 days or less.

Juvéderm 30 was found to provide a more persistent wrinkle correction than Zyplast over the 24-week course of the study. The percentage of subjects who maintained improvement with Juvéderm 30 at 24 weeks was 81% compared to 45% with Zyplast. At the conclusion of the study, 114 (78%) of 147 subjects expressed a preference for Juvéderm 30, while only 17 (12%) expressed a preference for Zyplast, and 16 (11%) had no preference.



Do the injections hurt?
Injections may cause some discomfort during and after the injection. Juvéderm 30 is injected directly into the skin using a fine needle to reduce injection discomfort. Physicians may choose to numb (anesthetize) the treatment area to further minimize discomfort.

What should I expect following the procedure?
Your physician will tell you what to expect following treatment with Juvéderm 30. Within the first 24 hours, you should avoid strenuous exercise, extensive sun or heat exposure and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites. If there is swelling, you may need to place an ice pack over the swollen area. You should ask your physician when makeup may be applied after your treatment.

Does the correction last forever?
No. Correction is temporary; therefore, touch-up injections as well as repeat injections are usually needed to maintain optimal correction.

What other treatments are available to me?
Other treatments for dermal soft tissue augmentation include bovine-based collagen and other hyaluronic acid-based dermal fillers. Aside from these treatments, additional options for the correction of lines and wrinkles do exist, including facial creams, BOTOX® Cosmetic, chemical peels, and laser skin surface treatments, and may be discussed with your physician.

When should I notify my physician?
Be sure to report any redness and/or visible swelling that lasts for more than a few days or any other symptoms that cause you concern to your physician and/or contact INAMED Product Support at (800) 624-4261.

For further questions and information please call 1-800-766-0171.

M#### .Rev ## MM/YY

JUVÉDERM® 30HV
Injectable gel

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

JUVÉDERM 30HV injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogenized gel implant. JUVÉDERM 30HV consists of crosslinked hyaluronic acid (HA) produced by *Streptococcus equi* bacteria, formulated to a concentration of 24 mg/mL, and suspended in a physiologic buffer.

2. INTENDED USE/ INDICATIONS

JUVÉDERM 30HV is indicated for injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds).

3. CONTRAINDICATIONS

- JUVÉDERM 30HV is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.

- JUVÉDERM 30HV contains trace amounts of gram positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.

4. WARNINGS

- JUVÉDERM 30HV must not be injected into blood vessels. Introduction of JUVÉDERM 30HV into the vasculature may occlude the vessels and could cause infarction or embolization.

- Use of JUVÉDERM 30HV at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present, should be deferred until the underlying process has been controlled.

- Injection procedure reaction to JUVÉDERM 30HV has been observed as consisting mainly of short-term inflammatory symptoms starting early after treatment and with less than 7 days duration. Refer to the ADVERSE EVENTS section for details.

5. PRECAUTIONS

- JUVÉDERM 30HV is packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged.

- Based on preclinical studies, patients should be limited to 20 mL of JUVÉDERM 30HV per 60 kg (130 lbs) body mass per year. The safety of injecting greater amounts has not been established.

- The safety and effectiveness of JUVÉDERM 30HV for the treatment of anatomic regions other than facial wrinkles and folds (e.g., lips) have not been established in controlled clinical studies.

- As with all transcutaneous procedures, JUVÉDERM 30HV implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.

- The safety of JUVÉDERM 30HV for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.

- The safety of JUVÉDERM 30HV in patients with known susceptibility to keloid formation, hypertrophic scarring and pigmentation disorders has not been studied.

- JUVÉDERM 30HV should be used with caution in patients on immunosuppressive therapy.

- Patients who are using substances that can prolong bleeding, such as aspirin, non-steroidal anti-inflammatory drugs and warfarin may, as with any injection, experience increased bruising or bleeding at injection sites.

- After use, treatment syringes and needles may be potential biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state and federal requirements.

- JUVÉDERM 30HV is a clear, colorless gel without particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe; notify INAMED Corporation at (800) 624-4261.

- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with JUVÉDERM 30HV, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if JUVÉDERM 30HV is administered before the skin has healed completely after such a procedure.

6. ADVERSE EVENTS

A. Clinical Evaluation of JUVÉDERM 30HV

In a randomized, controlled clinical trial to evaluate safety and effectiveness, 144 subjects were injected with JUVÉDERM 30HV in one nasolabial fold (NLF) and ZYPLAST® in the contralateral NLF. Pre-printed diary forms were used by subjects to record specific signs and symptoms experienced during each of the first 14 days (Day 0 through Day 13) after initial and touch-up treatments. Subjects were instructed to rate each common treatment response listed on the diary as "Mild," "Moderate," "Severe," or "None." Injection site responses reported by >5% of subjects in either treatment group are summarized in Tables 1 and 2.

Table 1 – Injection Site Responses by Maximum Severity Occurring in >5% of Treated Subjects (Number / % of Subject NLFs)

Injection Site Responses	TOTALS		JUVÉDERM 30HV (N*=144 NLFS)			Zyplast (N*=144 NLFs)		
	JUVÉDERM 30HV n‡ %	Zyplast n‡ %	Mild n‡ %	Mod† n‡ %	Severe n‡ %	Mild n‡ %	Mod† n‡ %	Severe n‡ %
Redness	129 90%	128 89%	61 42%	61 42%	7 5%	71 49%	42 29%	15 10%
Pain/Tenderness	129 90%	123 85%	68 47%	46 32%	15 10%	86 60%	32 22%	5 3%
Firmness	127 88%	122 85%	59 41%	53 37%	15 10%	62 43%	51 35%	9 6%
Swelling	124 86%	121 84%	61 42%	50 35%	13 9%	71 49%	41 28%	9 6%
Lumps/Bumps	120 83%	113 78%	57 40%	53 37%	10 7%	66 46%	40 28%	7 5%
Bruising	87 60%	69 48%	47 33%	33 23%	7 5%	38 26%	25 17%	6 4%
Itching	49 34%	51 35%	38 26%	9 6%	2 1%	39 27%	9 6%	3 2%
Discoloration	49 34%	43 30%	29 20%	15 10%	5 3%	31 22%	9 6%	3 2%

* Number of subject NLFs treated with the respective device
† Mod = Moderate
‡ Number of subject NLFs with each specific injection site response

Table 2 – Duration of Injection Site Responses Occurring in > 5% of Treated Subjects (Number / % of Subject NLFs)

Injection Site Response	JUVÉDERM 30HV (N*=144 NLFs) n† %				Zyplast (N*=144 NLFs) n† %			
Duration‡	≤3 Days	4-7 Days	8-14 Days	>14 Days	≤3 Days	4-7 Days	8-14 Days	>14 Days
Redness	56 39%	43 30%	10 7%	20 14%	53 37%	37 26%	13 9%	25 17%
Pain/Tenderness	59 41%	37 26%	25 17%	8 6%	55 38%	44 31%	17 12%	7 5%
Firmness	24 17%	29 20%	18 13%	56 39%	28 19%	26 18%	16 11%	52 36%
Swelling	31 22%	49 34%	21 15%	23 16%	53 37%	47 33%	13 9%	8 6%
Lumps/Bumps	32 22%	24 17%	19 13%	45 31%	15 10%	26 18%	14 10%	58 40%
Bruising	25 17%	31 22%	22 15%	9 6%	26 18%	29 20%	11 8%	3 2%
Itching	32 22%	9 6%	6 4%	2 1%	24 17%	18 13%	6 4%	3 2%
Discoloration	22 15%	11 8%	4 3%	12 8%	27 19%	5 3%	5 3%	6 4%

*Number of subject NLFs treated with the respective device
†Number of subject NLFs with each specific injection site response by maximum duration
‡Duration refers to number of days from symptom onset until resolution, irrespective of date of implantation.

Local injection site responses were recorded in subjects' diaries one or more times for 98% of JUVÉDERM-treated NLFs and 97% of Zyplast-treated NLFs. Subjects' scores for both products were predominantly Mild or Moderate in intensity, and their duration was short lasting (7 days or less). JUVÉDERM 30HV injection site responses reported by greater than 1% of subjects and not noted in the above tables were skin tingling and peeling. No clinically meaningful differences in the safety profiles of JUVÉDERM 30HV and Zyplast were found during the study.

B. Other Safety Data

In two additional randomized U.S. clinical studies of other JUVÉDERM formulations with a total of 295 subjects, the safety profile was similar to that described above for JUVÉDERM 30HV.

Post market safety surveillance of JUVÉDERM in countries outside the U.S. indicates that the most common adverse events include swelling, redness, discoloration, and bruising.

7. CLINICAL STUDY

A. Study Design

A prospective double-blind, randomized, within-subject controlled, multi-center clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM 30HV in the treatment of moderate to severe wrinkles. Subjects underwent treatment with JUVÉDERM 30HV in one NLF and the control implant (Zyplast bovine collagen) in the opposite NLF.

Up to 3 bilateral treatments (initial treatment and up to 2 touch-up treatments), approximately 2 weeks apart, were allowed. At 2 and 4 weeks after each treatment, the Independent Expert Reviewer (IER) assessed the level of correction achieved. If correction was less than optimal after the first or second treatment, the Investigator re-treated the under-corrected NLFs using the same respective treatment materials as in the initial treatment. The IER and the subject remained masked to the randomized treatment assignment.

Routine follow-up visits for safety and effectiveness occurred at Days 3 and 7 and Week 2 after each treatment, and at 4, 8, 12, 16, 20, and 24 weeks after the last treatment. Standardized facial photography was performed for documentation purposes. The Investigator and the IER independently evaluated the severity of the subject's NLFs using a validated 5-point (range 0 to 4) photographic NLF severity scale. The subject made independent self-assessments of NLF severity using a non-photographic 5-point grading scale.

B. Study Endpoints

The primary effectiveness end point for the study was the IER's NLF severity score over the post-treatment follow-up period. Effectiveness of device treatment was demonstrated by a lowering of the NLF severity score. Additional analyses included the subject's and the Investigator's live NLF severity assessments.

C. Subject Demographics

A total of 146 subjects (26 to 74 years of age) were randomized and treated, and 140 (96%) completed the 6-month follow-up period. Prior to enrollment, 80 (55%) had previous experience with other facial dermal treatments (e.g. alpha hydroxy agents, BOTOX® Cosmetic, microdermabrasion or retinoic acid).

Subject demographics and pre-treatment characteristics of the JUVÉDERM 30HV effectiveness population are presented in Table 3.

Table 3 – Demographics and Pretreatment Characteristics of the Effectiveness Population (Number / % of Subjects)
N = 146

Gender (Number / %)		
Female	132	90%
Male	14	10%
Ethnicity (Number / %)		
Caucasian	107	73%
African American	17	12%
Hispanic	20	14%
Asian	0	0%
Other	2	1%
Fitzpatrick Skin Phototype (Number / %)		
I	8	5%
II	34	23%
III	51	35%
IV	31	21%
V	18	12%
VI	4	3%
Mean Baseline NLF Severity Score*		
JUVÉDERM 30HV NLF	2.6	
Zyplast NLF	2.6	

*NLF Severity was ranked on a 5-point scale from None (0) to Extreme (4)

D. Effectiveness Results

The primary effectiveness results for JUVÉDERM 30HV based on the IER's assessment of NLF severity are presented in Table 4.

Table 4 – Effectiveness Summary
Independent Expert Reviewer's
NLF Severity Scores

		JUVÉDERM 30HV (N*=146 NLFs)		Control** (N*=146 NLFs)	
	n[§]	NLF Severity[†]	Improvement since Baseline[†]	NLF Severity[†]	Improvement since Baseline[†]
Baseline	146	2.6	–	2.6	–
Week 2	143	0.5	2.1	0.7	1.9
Week 12	129	0.9	1.6	1.7	0.9
Week 24	139	1.2	1.4	2.2	0.4

[*] Number of subject NLFs treated with the respective device
[**] A commercially available injectable bovine collagen implant
[§] Number of subjects NLFs with data at baseline and the specified time point
[†] Mean score

Throughout the 24-week study period, JUVÉDERM 30HV provided a clinically and statistically significant improvement in NLF severity. Clinical superiority was achieved at Week 24 for JUVÉDERM 30HV over Zyplast with mean NLF severity of 1.2 and 2.2, respectively (P <0.0001). Additionally, subject assessments for product preference favored JUVÉDERM 30HV: 84% preferred the JUVÉDERM-treated NLF over the Zyplast-treated NLF.

8. INSTRUCTIONS FOR USE

A. <u>To Attach Needle to Syringe</u>

- To assure proper needle attachment, use needles provided.
- Peel sealed cover off needle guard.
- Remove luer-lock end closure (tip cap) from syringe.
- Attach needle to syringe and twist to secure. Fully seat hub of needle in syringe. Do not over-tighten, as this may break the needle and/or dislodge the syringe.
- Pull off the needle guard to expose needle.

B. Physician Instructions

1. JUVÉDERM 30HV is a more highly crosslinked robust formulation, injected using a 27G needle for volumizing and correction of deeper folds and wrinkles. Prior to treatment with JUVÉDERM 30HV, the patient's medical history should be obtained and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration. Patients also should be advised that supplemental "touch-up" implantations may be required to achieve and maintain maximum correction.

2. The patient's soft tissue deficiencies should be characterized with regard to etiology, distensibility, stress at the site, and depth of lesion. Depending on the type of skin, best results are obtained when the defect is readily distensible and correction can be visualized by manual manipulation (stretching) of the skin. Pretreatment photographs are recommended.

3. Topical or injectable anesthesia may be used to manage pain during and after injection.

4. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be swabbed with alcohol or other antiseptic. Prior to injecting JUVÉDERM 30HV, depress the plunger rod until the product flows out of the needle.

5. The injection technique of JUVÉDERM 30HV with regard to the angle and orientation of the bevel, the depth of injection, and the quantity administered may vary. A linear threading technique, serial puncture injections, or a combination of the two have been used to achieve optimal results. If JUVÉDERM 30HV is injected too superficially, this may result in visible lumps and/or discoloration.

6. Inject JUVÉDERM 30HV applying even pressure on the plunger rod while slowly pulling the needle backwards. The wrinkle should be lifted and eliminated by the end of the injection. It is important that the injection is stopped just before the needle is pulled out of the skin to prevent material from leaking out or ending up too superficially in the skin.

7. The typical total volume of JUVÉDERM 30HV to achieve optimal correction is 1.6 mL per treatment site.

8. Correct to 100% of the desired volume effect. Do not overcorrect. The degree and duration of the correction depend on the character of the defect treated, the tissue stress at the implant site, the depth of the implant in the tissue and the injection technique. Markedly indurated defects may be difficult to correct.

9. If immediate blanching occurs, the injection should be stopped and the area massaged until it returns to a normal color.

10. When injection is completed, the treated site should be gently massaged so that it conforms to the contour of the surrounding tissues. If overcorrection occurs, massage the area

between your fingers or against an underlying superficial bone to obtain optimal results.

11. With patients who have localized swelling, the degree of correction is sometimes difficult to judge at the time of treatment. In these cases, it is better to invite the patient to a touch-up session after 1-2 weeks.

12. Patients may have mild to moderate injection site responses, which typically resolve in a few days. If the treated area is swollen immediately after the injection, an ice pack can be applied to the site for a short period.

13. After the initial treatment, an additional treatment of JUVÉDERM 30HV (from 1 to 2 weeks later) may be necessary to achieve the desired level of correction. If the wrinkle needs further treatment, the same procedure should be repeated until a satisfactory result is obtained. The need for an additional treatment may vary from patient to patient and is dependent upon a variety of factors such as wrinkle severity, skin elasticity and dermal thickness at the treatment site.

14. The physician should instruct the patient to promptly report to her/him any evidence of problems possibly associated with the use of JUVÉDERM 30HV.

C. Patient Instructions

It is recommended that the following information be shared with patients:

- Within the first 24 hours, patients should avoid strenuous exercise, extensive sun or heat exposure and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites.
- To report an adverse reaction, phone the Product Support Department, INAMED Corporation, (800) 624-4261.

9. HOW SUPPLIED

JUVÉDERM 30HV is supplied in individual treatment syringes with 27-gauge needles for single patient use and ready for injection (implantation). The volume in each syringe is as stated on the syringe label and on the carton. The contents of the syringe are sterile and non-pyrogenic. Do not resterilize. Do not use if package is opened or damaged.

10. STORAGE

JUVÉDERM 30HV should be stored at room temperature (up to 25°C / 77°F). DO NOT FREEZE.

JUVÉDERM 30HV has a clear appearance. In the event that a syringe contains material that is not clear, do not use the syringe; notify INAMED Corporation immediately at (800) 624-4261.

To place an order, contact INAMED Corporation at (800) 624-4261.

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